E2 Cont

Where Xaa is either any naturally occurring amino acid, or any amino acid except cysteine, m and n are chosen independently from the range of 2 to 20, the Xaa may be the same or different, and AA_1 is the same naturally occurring amino acid for all peptides in the library but may be any amino acid. Preferably, m and n are chosen independently from the range of 4 to 9.--

Please replace the paragraph beginning at page 91, line 26 with the following rewritten paragraph:

E3

--This example uses a eukaryotic cellular protein kinase as a target for which we have isolated artificial ligands. The peptide sequences shown above could easily be used to set up a screen for small molecules which bind at the same site. The artificial ligand could be used in any of the ways discussed in example 1. We could also use any other cellular enzyme as a target.. These selections may also be done in the presence of one or more cofactors or regulators of the enzymes function. In the case of PKC, we could have carried out the selection in the presence of diacyglycerol or phorbol esters to activate the enzyme. This would result in the enzyme taking on a different conformation and may alter the ligands that are obtained. This strategy may be altered to target a specific site by eluting the phage with the known ligand. To do this, we would carry out all of the binding and amplification steps as above, however, the elution step would be replaced by an extended incubation in the presence of large amounts of the natural ligand (i.e. Phorbol). Alternatively, the pool of phage from the final round of selection could be "sorted" by adding the natural ligand first followed by the phage. The binding of the natural ligand would prevent the phage binding to a specific site but not at others. We would then take the supernatant which contains the unbound phage and test individuals for binding. In this way you can